UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF MASSACHUSETTS

UNITED STATES *ex rel.* GREG THORPE, ET AL. [Consolidated] Plaintiffs, v. GLAXOSMITHKLINE PLC, and GLAXOSMITHKLINE LLC, Defendants	)	C.A. No. 11-10398-RWZ **FILED UNDER SEAL**

UNITED STATES' COMPLAINT

1. The United States brings this action to recover treble damages and civil penalties under the False Claims Act, damages and other monetary relief under common law and equity against the defendants GlaxoSmithKline plc and GlaxoSmithKline LLC (together "GSK") for causing the submission of false or fraudulent claims to federal health care programs.

2. From 1999 through 2010 in some instances, GSK engaged in a fraudulent scheme to deceive and defraud physicians, patients, regulators, and federal health care programs to cause prescribing and payment for certain of GSK's drugs. This conduct includes repeatedly publishing and promoting false and misleading accounts of studies and treatment guidelines to convince physicians to use GSK drugs. GSK misrepresented clinical evidence, downplayed or ignored safety risks, and failed to disclose the rejection by the United States Food and Drug Administration ("FDA") of some of the exact claims GSK was making to physicians. GSK promoted these products for uses that the FDA had not approved as safe and effective ("off-label" or "unapproved" uses), and for uses that were not medically accepted indications covered by federal health care programs. GSK also used a wide variety of gifts, payments and other forms of remuneration to induce physicians to prescribe GSK's drugs, including trips to Bermuda and Jamaica, spa treatments and hunting trips, and sham consulting fees.

3. GSK's fraudulent promotion of its drugs included the following:

(a) Promoting Paxil, an antidepressant drug, as safe and effective for children and adolescents, despite the lack of FDA approval for this use and three GSK clinical trials that failed to demonstrate Paxil's effectiveness while raising concerns regarding an increased risk of suicide among such patients.

(b) Promoting Wellbutrin SR ("WBSR"), an antidepressant drug, for unapproved uses including for children and adolescents, to treat Attention Deficit Disorder ("ADD"), Attention Deficit and Hyperactivity Disorder ("ADHD"), bipolar disorder, weight loss, obesity, sexual dysfunction, anxiety, and as an "add-on" therapy to other antidepressants, despite the fact that the drug was not demonstrated to be safe and effective for any of these uses.

(c) Promoting Advair, a combination of asthma drugs, for first-line use in mild asthma patients whose asthma could be controlled on one component alone—contrary to the FDA-approved label, specific FDA guidance, and established asthma treatment guidelines. In falsely claiming that Advair was superior to each of its components for this use, GSK relied on a study the FDA had specifically evaluated and rejected as showing superiority in GSK's application for an indication for this use.

(d) Promoting certain GSK drugs listed below with various forms of illegal remuneration, including cash payments disguised as consulting fees, expensive meals, weekend boondoggles, and lavish entertainment to prescribers and other health care professionals to induce them to prescribe and recommend GSK's drugs, including those paid for by federal health care programs, all in violation of the federal anti-kickback statute. 42 U.S.C. § 1320a-7b.

4. GSK's conduct, including its false and fraudulent statements, illegal promotion and payment of illegal inducements to prescribers, caused false or fraudulent claims to be submitted to federal health care programs for GSK's drugs, including claims for Advair, Paxil and WBSR, for uses that were not eligible for payment and for physician services relating to the prescribing of those drugs.

I. THE PARTIES

5. The United States brings this action on behalf of the federal health care programs the Department of Health and Human Services ("HHS") and the Centers for Medicare & Medicaid Services ("CMS"), which administers the Medicare and Medicaid programs.

6. This is the United States' Complaint as to the claims as to which it has intervened

in Civil Action Nos. 11-10398-NG, 03-10641-NG; 11-10741-NG, 11-10931-NG (D. Mass), which were filed by various relators and are consolidated as C.A. No. 11-10398-NG.

7. Defendant GlaxoSmithKline plc is a public limited company, incorporated under English law, with headquarters in Brentford, England. GlaxoSmithKline plc was formed in 2000 by the merger of GlaxoWellcome plc and SmithKline Beecham plc. It has operational headquarters in Research Triangle Park, North Carolina, and in Philadelphia, Pennsylvania.

8. Defendant GlaxoSmithKline LLC, a Delaware limited liability company, is the United States subsidiary of GlaxoSmithKline plc. GlaxoSmithKline LLC is the successor of SmithKline Beecham Corporation, which was the successor of SmithKline Beckman Corporation. GlaxoSmithKline LLC has headquarters in Philadelphia, Pennsylvania and Research Triangle Park, North Carolina.

II. JURISDICTION AND VENUE

9. This Court has subject matter jurisdiction under 28 U.S.C. §§ 1331 and 1345. The Court may exercise personal jurisdiction over GSK pursuant to 31 U.S.C. § 3732(a) and because GSK transacts business in the District of Massachusetts.

10. Venue is proper in the District of Massachusetts under 31 U.S.C. § 3732 and 28 U.S.C. § 1391(b) and (c) because GSK has transacted business in this District.

III. GSK'S OFF-LABEL MARKETING OF PAXIL

11. Paxil (paroxetine) is an antidepressant approved by the FDA for adults with major depressive disorder ("MDD" or "depression"), and other mental diseases.

12. The FDA has never approved Paxil to treat depression in children or adolescents under the age of 18. Nevertheless, from 1999 through at least 2003, GSK promoted Paxil for use in this population, while concealing the fact that Paxil failed to show efficacy on any of the primary endpoints in three controlled trials funded by GSK to study Paxil for this population. To

drive these promotional efforts, GSK touted a medical journal article that it paid to have drafted and that exaggerated Paxil's efficacy while downplaying risks identified during one of the trials.

13. The risks identified in GSK's trials, once uncovered, led the FDA to require in 2004 that GSK and other manufacturers of a class of drugs known as "selective serotonin reuptake inhibitors" ("SSRIs") place a "black box" warning on the labels of these products to warn doctors about the potential suicidality risks to children and adolescents. A black box warning is the strongest type of warning the FDA can require in a product label.

14. By misstating and exaggerating Paxil's efficacy and downplaying and concealing its risks during sales calls and promotional events, GSK misled the medical community about the risks and benefits of Paxil use in patients under 18 and caused false and medically inappropriate claims for Paxil prescriptions to be submitted to federal health care programs.

A. Three GSK Clinical Trials Failed To Demonstrate Paxil's Effectiveness In Treating Depressed Children

15. Between 1994 and 2001, GSK conducted three clinical trials of Paxil's safety and efficacy in treating depression in persons under 18. In all three studies, Paxil failed to reach statistical significance on the primary and secondary efficacy measures (or endpoints) in the study protocols. Due to these negative results, internally described as "disappointing" and "equivocal," GSK never sought FDA approval of Paxil for childhood or adolescent depression. As described below, GSK published false and misleading reports of these results, misrepresenting positive results while down-playing significant safety risks, including an increased risk of suicide in child and adolescent patients.

1. Study 329 Failed to Show Efficacy of Paxil for Children or Adolescents.

16. The centerpiece of GSK's efforts to market Paxil for childhood depression was the GSK funded Study 329, which ran from April 1994 to February 1998. This was a double-

blind, placebo-controlled study of the efficacy of Paxil in depressed children.

17. Study 329's clinical trial protocol contained two "primary" efficacy measures and five "secondary" efficacy measures. A "protocol" is a document created prior to commencement of the trial that describes the objectives, design, methodology, and statistical plan for the clinical trial. Pre-specified protocols are required by the FDA and scientific community to prevent post-hoc selection of favorable data and endpoints—i.e. "cherry-picking." A primary efficacy endpoint is a specific event or outcome that the clinical trial is designed to assess—such as whether a drug is more effective than a placebo in treating a condition. A "secondary" endpoint is typically related to the primary endpoint and may be of interest, but is not one the study is independently statistically-powered to assess.

18. The first primary endpoint in Study 329 was the degree to which a patient's Hamilton Rating Scale for Depression ("HAM-D") total score changed from a baseline. The HAM-D is a questionnaire to rate the severity of a patient's depression. The other primary endpoint: the patients' "response" to medication, as defined as (a) a 50% or greater reduction in the patient's HAM-D score, or (b) a HAM-D score of less than or equal to 8.

19. Study 329 did not show that Paxil was more effective than a placebo on either of its primary endpoints or any of its predefined secondary endpoints.

20. The 329 Study investigators later added several additional efficacy measures not specified in the protocol. Paxil separated statistically from placebo on certain of these measures.

2. Studies 377 and 701 Also Failed to Show Paxil Works in Patients Under 18.

21. In addition to Study 329, GSK conducted two other double-blind, placebo-controlled studies of Paxil for pediatric and adolescent depression: Study 377 from April 1995 to May 1998 and Study 701 from March 2000 to January 2001.

22. Like Study 329, both studies failed to demonstrate any statistically significant

difference in efficacy between Paxil and the placebo on any pre-specified primary or secondary endpoint. GSK noted in an internal report on Study 377, "the results failed to show any superiority for Paxil over placebo in the treatment of adolescent depression."

23. Internally, GSK acknowledged that its studies failed to provide sufficient support for the FDA to approve Paxil for childhood depression. In August 1998, six months after Study 329 closed, GSK noted in a Monthly Management Summary that:

> In both 329 (US) and 377 (EU) unable to detect a clinically or statistically significant difference between treatment groups in the prospectively defined primary variable - therefore no submission (MAA/NDA) for label indication for use of [Paxil] in Adolescent Depression.

24. Similarly in October 1998, GSK noted in a discussion of Studies 329 and 377:

> As you w[e]ll know, the results of the [329 and 377] studies were disappointing in that we did not reach statistical significance on the primary end points and thus the data do not support a label claim for the treatment of Adolescent Depression. The possibility of obtaining a safety statement from this data was considered but rejected. The best which could have been achieved was a statement that, although safety data was reassuring, efficacy had not been demonstrated. Consultation of the Marketing Teams via Regulatory confirmed that this would be unacceptable commercially and the decision to take no regulatory action was recently endorsed[.]

GSK concluded: "it would be commercially unacceptable to include a statement that efficacy had not been demonstrated, as this would undermine the profile of [Paxil]." Exhibit ("Exh.") 1.

25. As for Study 701, GSK noted in its final clinical report on that study that "[t]he results of this study failed to provide evidence for the primary and secondary endpoints that [Paxil] is more efficacious than placebo in treating children and adolescents with MDD."

B. <u>GSK Published an Article That Misstated Paxil's Efficacy and Safety for Children and Adolescents</u>

26. In April 1998, GSK hired Scientific Therapeutics Information, Inc. (STI) to prepare a journal article about Study 329. GSK worked closely with STI on the article by providing a draft clinical report to "serve as a template for the proposed publication,"

commenting on multiple drafts, and approving the final version.

1. In Publishing Study 329, GSK Falsely Claimed that It Demonstrated Paxil's Efficacy in Treating Depression in Patients Under 18.

27. The abstract of the article sent to JAMA stated that Paxil was "a safe and effective treatment for major depression in adolescents." The article, however, did not expressly identify the two protocol-specified primary efficacy measures—or that Paxil failed to show superiority to placebo on those two measures. Instead, the article claimed that there were eight efficacy measures and Paxil was statistically superior to placebo on four of them.

28. JAMA rejected the article in December 1999 and provided comments to the article's lead author, which he then circulated to GSK and STI. Some of the comments were extremely critical of how the article portrayed the study's results. One comment provided:

> [t]he major finding of this study was the high placebo response rate, nearly 50%. Paroxetine produced only a 20% higher response rate than placebo and then on some but not all of the scales used.... Readers of this paper might receive the wrong impression and believe that a 65 to 70% response rate could be achieved with paroxetine without the education and supportive psychotherapy that the placebo-treated patients in this study received. The outcome is particularly worrisome in this age of health cost containment. Thus, this study could do more harm than good unless the authors devote much more attention in their discussion to the fact that the bulk of the effect in this study was the result of good clinical management and not the medication.

Another noted that the "description of 'numerically superior' is not appropriate and results should be described as superior only when significant.... There is a bias in reporting [Paxil] results as numerically superior but failing to emphasize this is also the case for many of the outcome measures with imipramine."

29. Given the comments received, GSK and the lead author decided to revise the article and send it to what they called "a less demanding journal." GSK then worked closely with STI to revise and resubmit the article.

30. In June 2000, a revised version of the article was submitted to the Journal of the

American Academy of Child and Adolescent Psychiatry (JAACAP). In July 2000, JAACAP returned the article. Like JAMA, JAACAP questioned whether the article accurately characterized Study 329's results on Paxil's efficacy. For example, one comment stated:

> Overall, this is an important study due to its large size and its design of SSRI vs. TCA vs. Placebo. However, the results do not clearly demonstrate efficacy for [Paxil]. Therefore, the authors need to clearly note this.... [E]fficacy was not demonstrated for [Paxil]. It should be clearly noted that [Paxil] was not found to be superior to placebo on [three of the seven] completed measures of antidepressant efficacy in the Results subsection.

31. Another commenter noted the article obscured the primary endpoint results.

> The authors should clearly note that [three of the seven] outcome measures did not show [Paxil] was superior to placebo[.] Therefore the authors should not overstate the efficacy of [Paxil]. The fact that there was not a single a priori primary outcome measure is quite unusual for an industry sponsored study. If this is the case, this should be clearly noted as a methodological shortcoming. If there was a "primary" outcome measure, the authors should clearly note what that was.

32. GSK worked closely with STI to address the reviewers' comments and the article was resubmitted to JAACAP. JAACAP ultimately accepted the article in February 2001 and published it in July 2001. The article was titled "Efficacy of Paroxetine in the Treatment of Adolescent Major Depression: A Randomized, Controlled Trial." Exh. 2.

33. The final published article still mischaracterized the results of Study 329, even with the changes. Although Paxil failed to separate statistically from placebo on both the primary efficacy measures, as well as the five protocol-defined secondary efficacy measures, the article abstract flatly stated that "[Paxil] is generally well tolerated and effective for major depression in adolescents" and concluded that "[t]he findings of this study provide evidence of the efficacy and safety of the SSRI, [Paxil], in the treatment of adolescent depression."

34. Although the JAACAP article identified the study's two primary endpoints in the abstract, the article did not explicitly state that Paxil failed to show superiority to placebo on either of the primary efficacy measures (the only measures that the Study 329 was specifically

designed to assess). Instead, the article falsely stated that Paxil met one of the primary endpoints, noting how Paxil "separated from placebo at endpoint among four of the parameters: response (i.e., primary outcome measure)...." Since one of the protocol-defined primary endpoints was "response," the article's statement that Paxil "separated from placebo" on "response," falsely stated that Paxil had met that primary efficacy measure.

35. The final article's description of Paxil's performance on the protocol-defined secondary efficacy measures was also misleading. While the article abstract listed the five protocol-defined secondary endpoints, the text of the article omitted any discussion regarding three of the secondary measures on which Paxil failed to statistically demonstrate its superiority to placebo and instead focused on the five secondary measures that GSK added belatedly and never incorporated into the Study 329 protocol. The article claimed that these five secondary measures had been identified "a priori," thereby incorrectly suggesting that all the secondary endpoints discussed had been part of the original study protocol.

36. In short, the article distorted the study results and gave the false impression that the study's findings were primarily positive, when they were, in fact, primarily negative and as discussed below, contained a significant safety signal.

2. GSK Caused the JAACAP Article to Misrepresent and Minimize Paxil's Risks to Children and Adolescents.

37. At the same time that the JAACAP article exaggerated Paxil's efficacy for treating childhood depression, it downplayed the risks that Study 329 revealed. These risks eventually led the FDA to require all SSRI manufacturers to add a black box warning about the heightened risks of suicidality to adolescents taking Paxil and other drugs in the class.

38. An earlier draft of the JAACAP article (prior to the version ultimately published) disclosed that eleven (11) patients who had received Paxil had experienced serious adverse

events ("SAEs") potentially related to the drug. It stated:

> Serious adverse effects occurred in 11 patients in the paroxetine group, 5 the imipramine group, and 2 in the placebo group. An event was defined as serious if it resulted in hospitalization, was associated with suicidal gestures, or was described by the treating physician as serious. The serious adverse effects in the paroxetine group consisted of headache during down-titration (1 patient), and various psychiatric events (10 patients): worsening depression (2); emotional lability (e.g, suicidal ideation/gestures, overdoses), (5); conduct problems or hostility (e.g, aggressiveness, behavioral disturbance in school) (2); and mania (1). Of these, worsening depression, emotional lability, headache, and hostility were considered related or possibly related to treatment.

39. When JAMA rejected the article, one reviewer noted: "[T]here is a major omission from the tables. The serious adverse events should be at the top of any table of adverse events and these do not favor paroxetine. In fact, it is troubling that the authors do not note a significant increase in SAEs after paroxetine (but not IMI) relative to placebo." That comment was never addressed by GSK in the article. The JAACAP article had a table listing adverse events, but did not break out serious adverse events.

40. At the time GSK was circulating the draft article to JAMA and JAACAP, GSK had concerns about disclosing and publishing the increased serious adverse events associated with Paxil, particularly due to recent events in patients taking SSRIs committing violent acts, including the Columbine High School shootings.

41. GSK and STI instead revised the article to falsely state that only one of the 11 serious adverse events in Paxil patients was considered related to treatment—and failed to mention the fact that others had been listed by the study investigators as possibly related to treatment. The final article stated: "Of the 11 patients [who had serious adverse events while taking Paxil], only headache (1 patient) was considered related to paroxetine treatment."

3. The FDA Found Paxil Was Not Proven To Be Safe and Effective To Treat Children and Adolescents and Required Warning of the Risks.

42. In April 2002, GSK provided the FDA the results of its three pediatric depression

studies while attempting to gain an extension on Paxil's patent exclusivity period. In October 2002, the FDA informed GSK that the depression studies failed to demonstrate Paxil's efficacy in treating depression in individuals under age 18.

43. Moreover, the FDA asked for additional information about patients in the studies who had experienced adverse events and who had withdrawn from the study prematurely, as well as why GSK used the term "emotional lability" to describe the five patients who attempted to commit suicide or exhibited other self-injurious behavior. In May 2003, GSK for the first time provided the FDA with additional safety data from the studies.

44. Although GSK told the FDA there was no statistically significant difference in suicidality between placebo and Paxil in all the Paxil pediatric depression studies cumulatively, the difference between the potential suicide-related events among Paxil patients versus potential suicide-related events among placebo patients became statistically significant when the first 30 days after therapy were included in the analysis.

45. Likewise, upon closer examination the number of possible suicide-related events among the Study 329 Paxil patients increased beyond the five patients that GSK described in the JACAAP article as having "emotional lability." While collecting safety information for the FDA, GSK admitted that there were four more possible suicide-related events among Paxil patients in Study 329. In addition, the FDA later identified yet another possibly suicide-related event in the Study 329 Paxil patients, which also was not among the 11 serious adverse events listed in the JAACAP article. Thus, altogether, 10 of the 93 Paxil patients in Study 329 experienced a possibly suicidal event, compared to one of the 87 patients on placebo. This is a fundamentally different picture of Paxil's pediatric safety profile than the one painted by the JAACAP article, which listed at most five possibly suicidal events among Paxil patients, brushed those off as unrelated to Paxil, and concluded that treating children with Paxil was safe.

46. In June 2003, the FDA announced that although it had not completed its review of the data, it recommended that Paxil not be used to treat depression in patients under age 18.

47. In March 2004, the FDA issued a public health advisory requesting that SSRI manufacturers, including GSK, change the labels on their drugs to include "a [w]arning statement that recommends close observation of adult and pediatric patients treated with these agents for worsening depression or the emergence of suicidality."

48. In June 2004, the British Medical Journal published an article that accused the JAACAP article of "biased reporting." Regarding serious adverse events, the article said: "[D]espite five of these patients being admitted to hospital with events known to occur with the use of selective serotonin reuptake inhibitors, including suicidality, only one serious event (headache) was judged by the treating investigator to be related to paroxetine treatment. The criteria for determining causation of serious events were not stated."

49. In October 2004, the FDA directed GSK and other antidepressant manufacturers to include on their labels a black box warning to alert physicians about the potential for increased risk of suicidality in children and adolescents taking these drugs. The black box warning stated that "[a]ntidepressants increased the risk of suicidal thinking and behavior (suicidality) in short-term studies in children and adolescents with Major Depressive Disorder (MDD) and other psychiatric disorders." The FDA also required the labels to state:

> The risk of suicidality for these drugs was identified in a combined analysis of short-term (up to 4 months) placebo-controlled trials of nine antidepressant drugs, including the selective serotonin reuptake inhibitors (SSRIs) and others, in children and adolescents with major depressive disorder (MDD), obsessive compulsive disorder (OCD), or other psychiatric disorders. A total of 24 trials involving over 4400 patients were included. The analysis showed a greater risk of suicidality during the first few months of treatment in those receiving antidepressants.

50. In May 2006, GSK sent letters to physicians and updated Paxil's label to include an advisory regarding Paxil and suicidal tendencies in children, adolescents and young adults.

C. GSK Off-Label Marketed Paxil For Depression In Children and Adolescents

51. Despite the failure of its three clinical trials and the absence of FDA approval, GSK actively promoted Paxil to treat adolescent and childhood depression from 1999 to at least 2003. As reflected in internal GSK business plans, expanding Paxil's reach into the adolescent depression market was a key strategic goal well before the clinical trials were completed and well after GSK learned of the disappointing results of its three depression studies.

52. Likewise, notwithstanding Paxil's failure to meet the primary endpoints of Studies 329 and 377, GSK's 2000-2002 Paxil operating plan was to "[d]evelop/grow adolescent market by leveraging recently completed studies in adolescent depression and OCD."

53. Similarly, in 2000, a GSK consultant prepared a 32-page report titled, "Positioning Paxil in the adolescent depression market – getting a headstart." The purpose of the report, prepared at GSK's request, was "to assess the efficacy data relating to the use of Paxil for the treatment of depression and anxiety-related disorders in adolescents and to make recommendations on how to gain a headstart on the competition." The report acknowledged that "[t]he fact that Paxil failed to separate from placebo according to four of the outcome measures in the [329] study could be used as a weakness by competitors and may be an obstacle if filing for an extension of the product license." Nonetheless, the report recommended ways to spin the study to make Paxil the drug of choice in treating depressed children, including:

> If successfully managed, this initiative will extend use of Paxil to another population. There are 2.5 million adolescents suffering from depression in the USA. This represents a large market, though uptake is likely to be slow. To tackle this market would provide contact with a large number of psychiatrists who specialize in pediatrics.

54. In an August 2002 strategic brand plan, GSK continued to list pediatric use, including pediatric depression, as an opportunity for Paxil, even though it was four years after it knew the negative results of Studies 329 and 377, and a year after the results of Study 701.

1. GSK Provided its Sales Force Off-Label Information about Paxil for Children.

55. In September 1999, at a training for some of GSK's sales force promoting Paxil, Dr. Karen Wagner, a child psychiatrist, told the sales force that depression in adolescents was a lethal disorder that, if untreated, could lead to suicide and linger into adulthood. According to a GSK newsletter (Exh. 3), Dr. Wagner recommended Paxil for this population as follows:

> Obviously, therapy is needed and *Paxil* is one of the few pharmaceutical approaches that has safety and efficacy data to support its use in this [adolescent] patient population. And more data is on its way.
>
> As many of you know, [GSK] is preparing an indication for adolescent depression for *Paxil* next year! [GSK's] clinical study demonstrating the success of *Paxil* in treating depression among adolescents will be published in a peer reviewed journal during first quarter 2000.

56. According to the same GSK newsletter, Dr. Wagner discussed Study 329 (the results of which had not yet been published), explained that the results supporting Paxil use in pediatric patients were "statistically significant," and stated that "[a]s a result of this large study, we can say that [Paxil] has both efficacy and safety data for treating depression in adolescents."

2. GSK Provided the JAACAP Article to Its Sales Representatives.

57. In August 2001, the Paxil marketing team sent the JACAAP article to all 2,000 sales representatives who were selling Paxil, including 160 neuroscience specialty representatives. The article was accompanied by a cover memorandum created by a member of the Paxil marketing team ("Paxil cover memo"). This memorandum stated in bold type:

> **This 'cutting-edge,' landmark study is the first to compare efficacy of an SSRI and a TCA with placebo in the treatment of major depression in adolescents. *Paxil* demonstrates REMARKABLE Efficacy and Safety in the treatment of adolescent depression.**

(Emphasis in original). Exh. 4. The Paxil cover memo also stated that:

> Paxil was significantly more effective than placebo with regard to achievement of both HAM-D total score <8; CGI score of 1 (very much improved) or 2 (much

> improved), and improvements in the depressed mood items of the HAM-D and the K-SADS-L.

58. The memo further provided that Paxil "was generally well tolerated in this adolescent population, and most adverse events were not serious," and concluded:

> [T]he findings of this study provide evidence of the efficacy and safety of Paxil in the treatment of adolescent depression. Here's another example of GlaxoSmithKline's commitment to Psychiatry by bringing forth "cutting edge" scientific data. Paxil is truly a REMARKABLE product that continues to demonstrate efficacy, even in this understudied population.

59. Notably, the Paxil cover memo did not disclose that Paxil had failed to show statistical superiority over placebo for any of the study's protocol-specified primary and secondary endpoints. The memo did not say that adolescents in the study who received Paxil displayed more suicidal thinking and behavior than those who received a placebo. The memo did not say that GSK had completed two additional pediatric studies (Study 377 and Study 701), neither of which demonstrated that Paxil was effective in treating depression in children. The memo also did not say that Paxil was approved for use only in patients age 18 or older.

60. Although the Paxil cover memo noted that "[t]his article is for pharmaceutical consultants' information only" and instructed "Do not use it with, or distribute to, physicians," the memo's message was delivered to and used by the sales force to promote Paxil. The sales representatives and managers, who were all compensated and received bonuses based upon increased sales, including sales for off-label use in children, relayed the incorrect messages of the JAACAP article and Paxil cover memo to falsely promote Paxil as safe and efficacious for children and adolescents to health care providers around the country.

3. GSK's Sales Force Used the JAACAP Article to Promote Paxil Off-Label.

61. Relying on the Wagner lecture and JAACAP article, GSK sales representatives encouraged doctors to prescribe Paxil for children. GSK sales representatives documented their

doctor visits in "call notes" that were recorded in the notes that sales representatives' routinely prepared at or about the time of calls on prescribing physicians to record what had been discussed. These notes were available for review by managers as well as others representatives and reflect the one-sided picture that the sales force painted of Paxil's efficacy and safety for treating childhood depression. These call notes also demonstrate that the sales force ignored the Paxil cover memo's instruction not to use the JAACAP article with physicians.

62. The call notes written by GSK sales representatives repeatedly reflect their off-label promotion of Paxil, including the following:

> "Left water fountain. Reviewed [article on] Paxil adolescent MDD. Emphasized significance vs. placebo, study size. . . . Had reviewed article. Cited data to help underscore to parents/patients Paxil's utility here. Also important if liability an issue." *6/27/01 Milwaukee, WI*
>
> "Astros game. Discussed Paxil placebo and imipramine study in adolescents." *7/13/01 Houston, TX*
>
> "Detailed doctor on Paxil for major depression in adolescents and he agreed to use Paxil there." *6/1/01 Newark, OH*
>
> "Dinner and Yankee game with family. Talked about Paxil studies in children." *8/1/01 Westport, CT*

63. It was not until August 2003, after Great Britain contraindicated Paxil for children and the FDA warned doctors about possible suicide risks, that GSK for the first time asked its sales representatives to identify doctors on their call lists who treated patients under 18. As of May 2005, GSK had identified 5,800 child psychiatrists on the lists of physicians for Paxil representatives to target for Paxil promotions, including by providing samples. Of these, GSK confirmed that 1,324 were child-only prescribers.

4. GSK Promoted Paxil for Children by Giving Samples to Child Psychiatrists.

64. GSK also promoted Paxil for off-label uses by providing free Paxil samples to doctors who primarily or exclusively treated children.

65. GSK policies encouraged its sales representatives to provide samples to all doctors on their call lists. Because the Paxil call lists included doctors who primarily or exclusively treated children, GSK caused its sales representatives to give Paxil samples to doctors who were likely or certain to use the samples for unapproved uses.

66. GSK knew that its samples were being used in this manner, as illustrated by a survey of sales representatives which showed that the representatives wanted more smaller-dose Paxil pills, "which were used for children, elderly, and anxiety patients."

5. GSK Promoted Paxil for Children During Paxil Forum Meetings.

67. In 2000 and 2001, GSK also promoted Paxil for unapproved uses by bringing top-prescribing psychiatrists to lavish resorts for Paxil Forum meetings. There were four Forum meetings each year. Each representative attended two per year, and got to invite two psychiatrists to each meeting.

68. The meetings were held at expensive resorts such as the El Conquistador Resort & Golden Door Spa in Puerto Rico, the Rio Mar Beach Resort in Hawaii, and the Renaissance Esmeralda Resort & Spa in Palm Springs, California. GSK paid for the psychiatrists' lodging, air fare, and a $750 honorarium. GSK paid speakers a $2,500 honorarium. GSK also paid spouses' airfare if two cheaper tickets were available for the cost of one full-coach fare.

69. The psychiatrists typically arrived on a Friday morning. Presentations took place on Friday afternoon and Saturday morning. GSK hosted nice dinners on Friday and Saturday evenings and paid for entertainment including sailing, snorkeling, tours (e.g. the Bacardi rum distillery), golf, deep sea fishing, rafting, glass-bottomed boat rides, and balloon rides.

70. The actor/comedian GSK hired to emcee one of the meetings told the attendees "we have a wonderful and unforgettable night planned. Without giving it all away, I can tell you—you'll be experiencing a taste of luxury." One psychiatrist complained, "the style of the

conference would have been suitable for a convention of cosmetic sales reps; this is supposed to be a scientific meeting. To me, the music, lights, videos, emcees are offputting and a distraction (even demeaning)."

71. For many other psychiatrists, however, the Forum meetings seem to have had the intended effect. After the May 2000 Forum meeting in Hawaii, one psychiatrist wrote: "A beautiful location, enjoyable and fun-filled activities, an exciting, cutting edge, informative educational program, well-presented and organized, all add up to a most valuable and helpful experience – exhilarating!" Another doctor wrote after the Forum 2001 meeting in Palm Springs: "Both my wife and I enjoyed the extra care our drug rep gave to us all weekend."

72. Dr. Wagner spoke and recommended the use of Paxil for children and adolescents at one Forum meeting in 2000, three in 2001, and two in 2002. Before one meeting at which she spoke, a sales representative wrote to his supervisor that both of the psychiatrists he had invited "have high volume and are child specialists, which the program is devoted to."

73. GSK also used the meetings to relay its incorrect and misleading claims in the JACAAP article. GSK added Dr. Wagner to the agenda of a Paxil Forum meeting in June 2001 to "capitalize" on the impending JAACAP publication. Dr. Wagner's presentations during the Forum meetings were similar to the one she gave to the sale force. Dr. Wagner said adolescent patients who received Paxil in the 329 study showed "significantly greater improvement."

74. A GSK report of the 2000 meetings said that 12% of the attending psychiatrists said they would be more comfortable prescribing Paxil for children and adolescents as a result of the meeting. In written evaluations, numerous psychiatrists wrote that they would increase their Paxil prescriptions for children as a result of the meeting.

75. GSK tracked the Paxil prescription by doctors who attended the 2000 Forum meetings. "Results suggest that the Paxil Forum had a significant impact on Paxil market share

in the months after attendance," said a November 2000 memo for the Paxil marketing director. "Physicians grew actual market share versus their forecasted share immediately after Forum attendance. Test physicians grew market share significantly relative to Control physicians." The memo concluded that increased Paxil prescriptions due to the Forum 2000 meetings resulted in at least $900,000 in additional revenue in 2000 alone.

IV. GSK'S OFF-LABEL MARKETING OF WELLBUTRIN SR

76. WBSR is an antidepressant that has been approved by the FDA for only one use: the treatment of Major Depressive Disorder in adults eighteen years of age or older.

77. From 1999 through at least 2003, GSK engaged in a nationwide scheme to promote the sale and use of WBSR as safe and effective for indications, doses and populations that the FDA never approved as safe and effective, and that were not medically accepted indications. For example, GSK promoted WBSR for:

(1) weight loss and obesity;
(2) sexual dysfunction;
(3) Attention Deficit Hyperactivity Disorder (ADHD), Attention Deficit Disorder (ADD), bipolar disease and anxiety;
(4) addictions, including to drugs, alcohol and gambling;
(5) patients under age 18, including children;
(6) use as an add-on or in combination with other drugs;
(7) use as an antidote for the side effects of other antidepressant medications; and
(8) use in dosages contrary to that recommended in the label, with safety claims greater than those justified in the label.

78. GSK targeted the promotion of WBSR for unapproved uses especially in quality of life areas, e.g., enhancing sex life, losing weight, addressing substance addictions and attention issues. GSK promoted WBSR as what some sales representatives referred to as "the happy, horny, skinny pill." GSK did so knowing that much of the cost of the unapproved, non-medically accepted and/or inappropriate uses would be borne by federal health care programs.

79. GSK used the following tactics to achieve its marketing goals for WBSR:

(1) **Publicity Strategies:** GSK hired a public relations firm to hype small preliminary studies of WBSR for weight loss, obesity and sexual dysfunction in consumer and general news media to encourage WBSR sales for unapproved uses;

(2) **Speaker Programs:** GSK hired physicians to speak to other health care professionals and recommend unapproved uses for WBSR;

(3) **Details and Samples:** GSK encouraged sales representatives to provide one-on-one sales pitches ("details") to physicians about off-label uses of WBSR and distributed samples for uses not approved as safe and effective, such as samples to child psychiatrists and pediatricians for use in children;

(4) **"CME":** GSK sponsored ostensibly independent "medical education" events and/or medical society and grand rounds presentations on off-label WBSR uses where GSK effectively controlled topics, speakers, content, and participants; and

(5) **Inducements: Sham Advisory Boards, Trainings and Entertainment:** GSK used sham advisory boards, sham sales representative trainings and other forms of entertainment and remuneration to promote off-label usage of WBSR and induce doctors to prescribe WBSR.

80. While GSK promoted WBSR for unapproved, non-medically necessary and/or inappropriate uses, GSK also took steps to evade detection by government agencies and conceal the real purpose and nature of activities, including making repeated false statements to the FDA about the conduct and concealing the documents that demonstrated the conduct.

A. GSK's Corporate Plans Set Forth Its Intent to Promote WBSR for Unapproved Uses

81. In a variety of national and regional strategy documents, GSK reflected its corporate strategy to promote the use of WBSR for unapproved uses.

1. GSK Hired A Public Relations Firm to Create Buzz and Drive Sales of WBSR for Off-Label Uses.

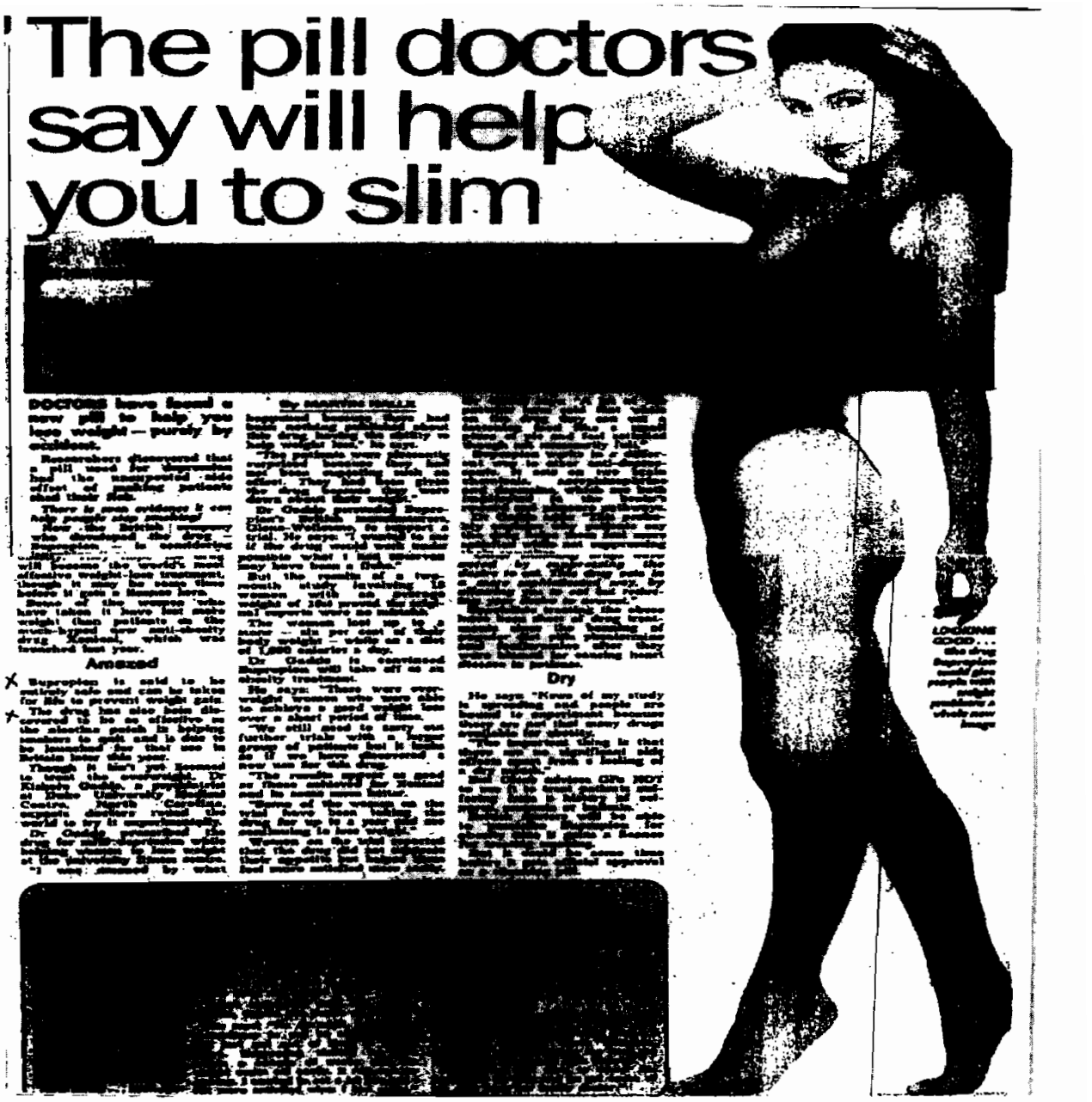
82. In 1998 and 1999 and through at least 2002, GSK used media plans as part of its marketing strategy to promote WBSR. These media plans were designed to "create [a] buzz" and to publicize off-label uses of WBSR, such as for weight loss or sexual dysfunction in non-depressed patients. Exh. 5.

83. For example, GSK hired the Cooney/Waters Group ("Cooney/Waters"), a public

relations firm, to promote and publicize a GSK-funded pilot study by Dr. Kishore Gadde of Duke University on the use of WBSR in non-depressed obese patients. Although the pilot study included only 25 patients who were on the drug for only eight weeks, GSK and Cooney/Waters promoted the study in the mainstream media and fostered the coverage of WBSR as a diet pill. This promotion included preparing and distributing a press release about the study to general consumer magazines (such as Allure and Redbook), providing Dr. Gadde with media training, and coordinating with the media "to make sure reporters and editors have the new data and understand its significance." Given the limitations of the study and preliminary nature of the data, its "significance" should only have been to researchers considering further research, not to the general public.

84. Cooney/Waters and GSK's efforts generated stories from CNN and Dateline, as well as tabloids. Exh. 6. It resulted in articles with headlines such as "Bigger than Viagra? It sounds too good to be true: a drug to help you stop smoking, stay happy and lose weight" and "Now *That* is a Wonder Drug." As Cooney/Waters itself touted in a September 1999 report to GSK (Exh. 7), its efforts to promote Gadde's "weight study has been carried by: [ ] More than 70 local television stations [ ] More than 50 local newspapers and consumer magazines nationwide and in the United Kingdom [ ] More than 9 Internet outlets nationwide [ ] 12 trade publications in the United States [and] Media impressions exceed[ed] 15 million (not including wire and Internet impressions)."

85. One example of the media pick up included the following article in the tabloid "The Sun":


The pill doctors say will help you to slim

86. GSK also hired Cooney/Waters to publicize results of other off-label studies to general and consumer media, including a small study of WBSR to treat sexual dysfunction, and a later study of WBSR for weight loss in patients with depressive symptoms but not depression.

87. GSK also hired Dr. Drew Pinsky from MTV and Loveline as a spokesperson to deliver messages about WBSR in settings where it did not appear that Dr. Pinsky was speaking for GSK. GSK indirectly paid Dr. Pinsky $100,000 in March 1999 and $175,000 in April 1999.

Exh. 8. In about June 1999, Dr. Pinsky spoke on a national radio program and communicated key GSK WBSR campaign messages. The "Highlights" included: "Switching to or adding Wellbutrin is recommended for people experiencing a loss of libido." During the program, among other things, Dr. Pinsky noted that the drug in WBSR, bupropion, could explain a woman suddenly having 60 orgasms in one night. Dr. Pinsky explained that one of the things he advocates for people experiencing diminished libido or arousal is WBSR. Exh. 9.

88. According to a report prepared on behalf of GSK in 2002, the media campaigns surrounding use of WBSR for obesity, weight loss and sexual dysfunction reached a total audience of more 387 million, "[s]parked sales growth" and caused WBSR to be used increasingly as a first-line product, both alone and in combination with other therapies. Exh. 10

B. Follow-Up on Gadde Study

89. Following the pilot study by Dr. Gadde on the use of WBSR for obese non-depressed women, GSK hired Dr. Gadde and other weight loss specialists to give promotional talks on behalf of GSK to other physicians and to discuss the use of WBSR as a "weight-loss agent." In these talks, the speakers reviewed the use of WBSR for weight loss in non-depressed patients and advocated its use for weight loss, despite the lack of FDA approval or substantial evidence supporting this use. In such programs, Dr. Gadde, a consultant for the Duke Diet and Fitness Center, presented his study on the use of WBSR in non-depressed patients.

90. However, in the spring of 2000, when Dr. Gadde was preparing the manuscript about the study for publication, GSK had a falling out with him over his insistence on emphasizing certain safety warnings and his refusal to use Wellbutrin SR's trade name.

91. Dr. Gadde was informed by a chairperson at his university, also a GSK consultant, that GSK would not fund any more of Dr. Gadde's studies due to his refusal to remove some of the safety discussion from the article. GSK's Clinical Director for their Central

Nervous System program, Tim Kuhn, also informed Dr. Gadde in writing that Dr. Gadde should not have made the decision to submit his own article on the study to the journal Lancet rather than JAMA without consulting with GSK as GSK was his "partner in publishing decisions that consider both patient and brand issues." Kuhn explained to Dr. Gadde the consequences of such a failure to consult with GSK: "It is unlikely that additional support for other investigator-initiated projects will be embraced enthusiastically if there is no input from GW [GlaxoWellcome, GSK's predecessor] or if input from GW is not considered." Exh. 11.

92. After this falling out, GSK's national marketing team increasingly utilized other physicians, including Dr. Ken Fujioka, an endocrinologist specializing in weight loss treatments, as its spokespeople to present the Gadde study, rather than Dr. Gadde himself.

93. GSK hired Dr. Fujioka in September 2001 to train the WBSR sales force on using WBSR for weight loss. Dr. Fujioka is known as the "Fat Doctor" due to his focus on diet and weight loss. Dr. Fujioka does not treat depression and thus does not even utilize WBSR for its only on-label use. Dr. Fujioka's talk on the effects of WBSR on weight included slides claiming WBSR is associated with significantly more weight loss than placebo and that 77% of patients treated with WBSR 400 mg/day achieved more than 5% weight loss. This presentation also included claims about the effectiveness of WBSR to treat obesity in non-depressed patients.

94. GSK sales force members utilized Dr. Fujioka in programs and sales calls to discuss the weight loss effects of WBSR. Some examples of the call notes reflecting GSK's sales force use of Dr. Fujioka include:

> "SIB program with local KOL's and visiting KOL's (Ken Fujioka). Goodman presented on WSR in ADHD and Depression, outstanding job, Fujioka presented the weight data which sparked alot of participation from the audience as well as feedback . . . ." *11/3/01 Durham, NC*

> "Followed up on sib. Enjoyed. Liked Fu[j]ioka talk benef of lbs w/ wsr." *10/26/01 Hudson, FL*

"she loved fujioka..invited her to hear hudziak in january" *11/26/01 Brockton, MA*

"Dr Fujioka lecture on weight studies in Boston. Send him info on the use of methadone and WSR." *11/9/01 Lynn, MA*

"She came to the Fujioka program and I would expect to see her WSR numbers increase based on the weight loss data he presented tonight. . . . thought we should really spread the word about these studies" *3/21/02 Redwood City, CA*

"he says dr fujioka was great- he walked out of his office after the tele conf and implimented options he spoke about." *6/27/02 Bangor, MA*

C. Operation Hustle: National Campaign for WBSR to Treat "Co-Morbidities"

95. In 1999, GSK also instituted "Operation Hustle" - a national sales campaign. In meetings with national sales and marketing personnel in about 17 cities around the country, GSK introduced a new approach to selling WBSR by promoting WBSR for "co-morbid conditions" that were not FDA-approved uses for WBSR, but may also exist in depressed patients, such as weight gain, sexual dysfunction, and ADHD. GSK instructed its sales force to promote WBSR as increasing the neurochemical agents norepinephrine and dopamine, and thus effective in treating "co-morbid" disorders thought to be connected to levels of norepinephrine and dopamine, such as ADHD, addiction, and craving.

96. In April 2000, GSK's strategic plan for WBSR identified as sales opportunities off-label uses such as ADHD, anxiety, lethargy and bi-polar disorders and listed WBSR use in combination with other antidepressants to their treat side effects as a growth opportunity.

97. GSK's off-label marketing strategies worked. Less than a year later, GSK noted that WBSR's "use for treatment of antidepressant induced sexual dysfunction has increased due to product positioning," and that it was a "[p]roduct of choice for adding . . . patients who experience sexual dysfunction or efficacy poop-out." Sales increased approximately 34% from 2000 to 2001, far in excess of the market rate of growth for antidepressants.

98. Sharon Sharo, the Director of WBSR Marketing, presented to the management team the plans for WBSR for 2001 and included as WBSR "Growth Drivers for 2001":

- Completed 2 Obesity trials - results presented [at conferences] . . .
- Obesity study investigating the efficacy and tolerability for WBSR in overweight and obese women published in Obesity Research 9/01 (Gadde).
- WBSR was effective and well tolerated for weight loss at 8 weeks with sustained [sic] the weight loss through the continuation phase.

99. Sharo also explained that GSK's objectives of speaker training for WBSR included "Present and position Gadde and Anderson weight data" despite the fact that the weight data was both off-label and extremely preliminary. She also noted that the December 2001 Speaker Training in Fort Lauderdale, Florida would include a key talk by Dr. Fujioka.

100. In August 2001, GSK's Strategic Brand Plan for WBSR noted under "opportunities" an "increased awareness of sexual dysfunction and legitimacy of treatment of sexual dysfunction in non-depressed patients." The Brand Plan also stated that GSK will "[a]ggressively support the efficacy and utility of WBSR with new clinical data" and "[t]hrough non-promotional means (MI letters, publications etc.) optimize use of strong clinical data for prevalence of antidepressant induced sexual dysfunction, comparison vs. key competitors in depressed and non-depressed patients for weight loss and HSDD."

101. GSK also pushed throughout the company the message to promote WBSR as an "add-on" drug to treat co-morbidities (i.e., side effects of other drugs) and for combination therapy. For example, in a 2002 Business Plan forwarded by a Regional Sales Director in the New England Region, a manager set forth the following strategy to grow market share:

> Increased focus on D1 Medicaid High potential Prescribers: Target Medicaid areas with strong messages about the benefits associated with NE and DA (the components of WBSR) (i.e. LOW sexual dysfunction, impact on weight, cognition, lethargy and smoking cessation . . . Develop Medicaid Champions to

> disseminate WBSR messages . . . increase the switching/adding for sexual dysfunction.

102. Other business plans also encouraged growing WBSR sales by utilizing "weight loss data" and promoting the product as "add-on therapy to SSRI." These plans also included a specific focus on physicians prescribing for Medicaid patients.

D. GSK Used Speaker Programs to Promote WBSR for Unapproved Uses.

103. GSK used speaker programs to spread off-label information about WBSR. GSK trained and paid physicians to speak to other physicians at thousands of promotional events per year that were organized by GSK's sales representatives and managers. Many of these events included false and/or misleading claims about WBSR's safety and efficacy for unapproved uses. In these talks on behalf of GSK, the speakers recommended WBSR for a wide variety of unapproved uses, including for weight loss, to treat sexual dysfunction, ADHD and other attention disorders, and even for patients with bulimia or who were abruptly discontinuing alcohol (both of which were specifically contraindicated in WBSR's labeling).

104. GSK paid physicians to attend lavish meetings, in places such as Jamaica, during which GSK promoted WBSR for off-label uses. These meetings were intended to reward physicians who were writing a large number of WBSR prescriptions and induce physicians to write more WBSR prescriptions, including for unapproved uses. Sales representatives' call notes reflect the off-label discussions and purpose of these meetings:

> "Jamacia Discussed role of WSR in treating depression, ADHD, and obesity" *1/27/01 NY, NY*

> ". . . Wellbutrin Speakers Training – Jamaica – Interacted several times. He was interested in meeting someone from Marketing about soft money – I told him to talk to [Marketing Director] Lafmin Morgan – which he did." *1/28/01 Durham, NC*

> "really enjoyed Jamaica – told of successfully using Welb in pt w/ADHD" *1/30/01 Minneapolis, MN*

> ". . . had a wonderful time in jamaica with well sr marketing. spent some time with tom and bill which was great. he is eager and ready to talk for us. numbers are reflecting a large increase in new rx's... i think he gets the picture. sched. a reprint mastery for the group in his office on the 16th . . ." *1/31/01 Quincy, MA*

105. In late 1999 or early 2000, GSK established a national WBSR speaker program known as PRIDE (Peer Review of Intimacy, Depression and Efficacy) that featured many off-label speakers. GSK determined that its PRIDE dinner programs yielded an approximate 280 percent "return on investment."

106. GSK representatives, including managers, attended every PRIDE program. GSK obtained copies of the presentations and invited to speak most frequently those speakers who effectively promoted off-label uses of WBSR. Sales representatives and managers invited the key speakers back to speak over and over again across the country and touted them to their colleagues, sometimes precisely because of the off-label messages and their ability to increase sales of WBSR.

107. GSK paid such speakers in the range of $1,000 to $2,500 for a one hour program. Because many of the speakers traveled the country making virtually identical presentations at each location, little or no additional preparation time was necessary. Moreover, the same speaker might be paid three times a day for making the same or similar presentation at breakfast, lunch and dinner in a single day. Some speakers would not even agree to come to a territory to speak unless they were guaranteed a "six pack" of speaking events at approximately $2,000 each, for a total of at least $12,000 for the two day trip. This amount far exceeded the amounts they were otherwise paid to practice medicine or lecture as university professors.

1. Dr. James Pradko

108. Dr. James Pradko was one of GSK's top WBSR speakers from 2001-2003. From 2001 to 2002, he was paid half a million dollars per year for speaker programs about WBSR and

nearly a million dollars in 2003 alone. Dr. Pradko was also hired by GSK to present at sales representative training sessions—both initial and advanced sales training—and was repeatedly a presenter at GSK's WBSR National Speaker Training Meetings. Dr. Pradko, whose specialty is family practice, was also appointed to GSK's National Advisory Board.

109. Dr. Pradko traveled to every GSK sales region to present his standard presentation, "The Neuroreceptor Basis of Initial Antidepressant Choice." In 2002, Dr. Pradko made this presentation at more than 300 promotional speaker events.

110. Dr. Pradko's presentation was permeated with off-label claims about WBSR. Among other claims, Dr. Pradko represented that WBSR could be used for weight loss, ADD in pediatric patients, chronic fatigue syndrome, marital dysfunction, erectile dysfunction, addictions and chemical dependencies, attention disorders, low energy in anxious patients, sleep disorders, restoring REM levels of sleep, restoring libido and a healthy sex life, and treatment of pregnant women. Dr. Pradko also told attendees that WBSR could be used as an "add-on" to treat SSRI side effects such as "poop out", sexual dysfunction and weight gain.

111. Many of Dr. Pradko's claims were contrary to WBSR's label. For example, Dr. Pradko asserted that he put all of his pregnant patients on WBSR and further claimed that the FDA said that it is safest antidepressant in pregnancy. WBSR's prescribing information, however, specifically cautioned that the drug "should be used during pregnancy only if clearly needed" and that "there are no adequate or controlled studies in pregnant women." Moreover, after animal studies were done, the FDA updated the label for WBSR in March 2007 to Pregnancy Category C because "it did appear to cause harm to the fetus in previous animal studies." According to the updated label, "[i]n these studies, there was an increased risk of birth defects and lower fetal weights when the medication was given to pregnant rabbits."

112. Dr. Pradko's recommendations to use WBSR use in treating sleep disorders are

likewise called into question by WBSR's label. The label cautions that in placebo-controlled trials, between 11 and 16 percent of patients receiving WBSR experienced insomnia. Even GSK's own marketing department recognized that "[i]nsomnia is a common concern/comorbid condition within the depressed patient population and bupropion [the operative molecule in WBSR] is associated with increased insomnia."

113. Similarly, Dr. Pradko's claims advocating WBSR use in pediatric patients contravene the drug's FDA approval, which was approved only for patients 18 and older. GSK's prescribing information warned that the safety and effectiveness of WBSR in pediatric patients has not been established. Moreover, as noted above, in October 2004, the FDA required all antidepressants including WBSR to carry a black box warning that describes the increased risk of suicide and suicidal thoughts and behavior in children and adolescents given antidepressants.

114. Despite its off-label content, GSK managers around the country and at headquarters enthusiastically embraced Dr. Pradko's messages and his standard talk using a baseball analogy known as the "baseball diamond talk." Sales representatives repeated and reinforced Dr. Pradko's off-label messages in their calls upon physicians. For example, in July 2000, a northeast marketing development manager emailed the national brand directors:

> First of all, congrats to you and your entire WSR team on a great WSR Univ.! Using Dr. Pradko's baseball graphic of neurotransmitters, you guys have hit a grand slam. The numbers, the incremental growth, what a success story. (Now I know why you called them "PRIDE" programs.)

115. In addition to live speaker programs, GSK actively promoted Dr. Pradko's off-label messages with an audio cassette version of his lecture. From at least 2000 until into 2003, GSK purchased and distributed to physicians hundreds, if not thousands, of audiocassette tapes of Dr. Pradko's standard lecture with the off-label marketing messages (the "Pradko tape"). The sales force reflected this and the impact on sales in their call notes, including the following:

"Raved about Pradko (could hear better on tapes than at program in A.C.) and the fact that he has increased his WSR use EVEN MORE!!!! in certain types of pts." *4/25/01 Vineland, NJ*

"followed up w/ pradko tape, dr was so happy to have it, wants bubble sheets too, scheduled to speak to corporations in the area in march, reminder on wt loss data, adding sr, & first line therapy" *2/11/02 Bridgewater, NJ*

"Stressed the Pradko Tape and he said she will listen to it on the drive back home tonight and he liked the analogies and he said he had just written for the 150 for 13yr ld girl that was on adderall and becoming combative but doing better with the add. He said he is starting slower and lower and seeing better compliance to start it out." *10/29/02 Wellston, MI*

"told about morning program with pradko in march. has listened to half the pradko tape already and said he would come to the program." *1/28/03 Battle Creek, MI*

"She raved about the Pradko tape, has listened to it 3 times, much less commercial than the teleconference, loved the information, uses it daily now. I also gave her WSR bubble sheet tear-offs, which she likes and will use. Finally went over XL coming – very interested in this." *6/11/03 Grand Rapids, MI*

"went through all products and then went through all reasons to use well xl and 100% conversion. pradko tapes and he said he would go to the program." *10/22/03 Smyrna, GA*

116. In the spring of 2002, a GSK marketing development manager worked with Dr. Pradko to prepare a DVD of Dr. Pradko's standard talk. GSK paid for the development costs. Although the DVD purported to be independent medical education, it was in fact the promotional talk Dr. Pradko gave on behalf of GSK and developed into a DVD at GSK's request.

117. Dr. Pradko provided the DVD to the southeast region of GSK for a pilot project, with the hope that the company would purchase the rights to use the DVD nationally. The Regional Sales Director at the time, Anne Whitaker, supported the project and accompanied a sales representative to a physician's office to view the DVD. Although Whitaker observed the content of the DVD at that time, including the off-label messages it contained, her team continued to distribute and play the DVD for physicians around the region.

118. In one month, GSK sales representatives in the southeast played this DVD for

physicians approximately 900 times. The representatives raved about the "independent" CME DVD's effectiveness in persuading physicians to prescribe WBSR with comments such as "This DVD has been the best selling tool for me yet. It has not only helped me reach customers that would not attend programs but also teach myself and customers the best way to use [WBSR]."

2. Dr. James Hudziak

119. In standard presentations that were delivered hundreds of times at GSK PRIDE and local speaking events, Dr. James Hudziak, a child psychiatrist, advocated using WBSR for a wide range of off-label treatments including ADHD, addictions, sexual dysfunction, obesity, weight reduction, bi-polar disorders, addictions and bereavement. Dr. Hudziak's off-label messages were in slide presentations he provided to GSK prior to his talks on behalf of the company. Sales representatives were thrilled with the impact of Dr. Hudziak's off-label messages, as reflected in their call notes, including the following:

> "Lunch with the group today. we dsicussed the use of WSR to treat ped with ADD and ADHD problems. I used the Hudziak and Wilens articles to discuss WSR advantages. They all agreed." *5/10/01 Atlanta, GA*
>
> "Follow up on Hudziak SIB. He thought Hud was interesting and wanted to read everything Hud talked about. Need to follow with all the studies mentioned in the SIB, probably Sex Monograph, Rush, etc." *4/22/02 Marion, OH*
>
> "disc what hudziak says in regard to wsr and adhd." *9/9/02 Franklin, TN*
>
> "hudziak approp pt profile for obese/smokers adhd/weight loss potential, the higher the BMI, the more you'll lose – said he would try" *9/10/02 Clearwater, FL*

120. Not everyone was as impressed with Dr. Hudziak, however. According to one sales representative, one physician who attended "thought [Dr. Hudziak] was a drug whore."

121. Dr. Hudziak's talks and messages were well-known to senior managers at GSK. His slides were circulated among the members of the sales force, including to managers. He spoke at both speaker trainings and national advisory boards. Senior marketing managers

attended his talks. GSK managers around the country regularly booked Dr. Hudziak for speaker engagements and repeatedly encouraged others to book him in their regions, even though they knew his slides and presentation contained off-label information.

122. WBSR Brand Director Lafmin Morgan and Regional Sales Director Mike Delea attended Dr. Hudziak's GSK sponsored talk in connection with the arrival of the Tall Ships flotilla in Boston in the summer of 2000. Delea congratulated the team that organized the event noting that "Dr. Hudziak gave a solid presentation on the effectiveness of [WB]SR. The weather was perfect, along with the boat cruise and viewing of the Tall Ships." Exhs. 12-15.

123. Sales representative comments concerning this event include the following:

> "wants to go to the 4pm tall ships. ... - will get back to him if we decide agst kids. don't think we will.... numbers are way to imp. to us." *06/20/00 Boston*
>
> "confirmed 3 tix for tall ships for doc and kids." 07/07/00 Randolph, MA
>
> "Still talking about Bermuda trip. Wants to play golf at Ipswich CC. Setting it up for Sept. Looking forward to Tall Ships." *07/13/00 Salem, MA*
>
> " . . . r/t Hudziak program in Providence in Jan. Said she & Dr. had heard him at Tall Ships and Dr. loved him. Her prescribing in growth track show this!" *12/15/00 New Bedford, MA*

124. Dr. Hudziak was also a popular moderator for advisory boards. He was hired by GSK to lead numerous local and Special Issue Boards, where he presented off-label information and encouraged other physicians to use WBSR for on and off-label uses.

125. For example, Dr. Hudziak was a featured speaker at a Regional Advisory Board for the northeast region in August 2000 at the Fairmont Princess Hotel in Bermuda. Dr. Hudziak was paid $5,000 and he and his wife were treated to accommodations and entertainment for the weekend, which Dr. Hudziak described as a vacation. Exhs. 16-18.

126. The GSK manager who organized the event solicited input from the GSK sales force as to which doctors to invite in order to impact sales. He asked managers to nominate

attendees by providing information on their key "customers" (physicians), those customer's prescribing habits and what the sales manager would "wish to achieve with [the] customer . . . in an effort to obtain the greatest ROI [Return on Investment] . . . ." Exh. 19.

127. GSK then selected doctors to attend in order to impact their prescribing of GSK drugs. The organizers were provided instructions the sales team's goals for each physician, including ways to increase their use of WBSR off-label. For example, the sales team noted that one doctor "is very pleased with the use of WBSR especially with its effectiveness in ADHD. Please utilize his positive experience and enthusiasm of WBSR to influence other clinicians." For another: "Dr. [N] is a Child Psychiatrist and I would like the safety and efficacy of a first line antidepressant and treatment option for ADHD to be relayed to him." Exh. 20.

128. One physician was told that he was invited to "sit for 4 hours, share your thoughts around WSR, get paid at a nice place in Bermuda" and he was invited because he was "the number one potential doc in the entire state of Maine prescribing anti-depressants." The event included a four-hour meeting in three days in Bermuda. By noon Saturday, the "work" was done and GSK provided meals, activities and an evening dinner cruise. Exh. 21.

129. The Bermuda meeting presentations included numerous recommendations for off-label uses of WBSR by Dr. Hudziak. Moreover, sales force statements before and after the meeting demonstrate the purpose of the meeting was really to encourage prescribing of WBSR, and not to gather needed consulting about WBSR, including:

> "will be attending rabs program in Bermuda 8/11-8/13: low market share but high volume target. . ." *07/05/00 Westerly, RI*
>
> "She spoke highly of their trip to Bermuda and of riding around on a scooter! She like Hudziak's talk, and is increasing her usage of SR." *02/01/01 Greenland, NH*
>
> "He attended the Bermuda RAB this past August and he has increased his prescribing of WellSR" *12/13/2000 email re: Marlborough, MA physician*

130. Dr. Hudziak was also a speaker selected by GSK for ostensibly independent CME events relating to WBSR. In fact, in the summer of 2002, Dr. Hudziak expressed concern because a new Vermont law required him to report the large amount of compensation that GSK paid him to speak on its behalf. To avoid disclosing how much he was receiving from GSK, Dr. Hudziak informed GSK that he would only do CME events, not promotional events.

131. GSK therefore arranged a series of purportedly independent "CME" events where GSK scheduled the event and selected the speaker (Dr. Hudziak) but arranged for a CME vendor, Primary Care Network, to "accredit" the events.

3. Other Physician Speakers

132. Besides Dr. Pradko, Dr. Hudziak, Dr. Gadde and Dr. Fujioka, many other GSK physician speakers for WBSR also used presentations that promoted off-label uses. These doctors were paid by GSK for such speaking engagements and spoke at GSK-sponsored events.

133. For example, Dr. Norman Sussman's standard PRIDE presentation incorporated representations that WBSR promotes weight loss, including in non-depressed patients. Dr. Sussman also advocated using WBSR to treat ADHD, smoking cessation, SSRI side effects, chronic fatigue syndrome, restless sleep, and Parkinson's disease.

134. Dr. Sussman also made claims that improperly minimized or contradicted the drug's FDA-approved label. Dr. Sussman represented that WBSR's seizure rates were either equivalent to or less than the rates seen with SSRIs, even though no head-to-head trials studied comparative seizure rates and the seizure rate listed for WBSR in its label is higher than some other antidepressants. Likewise, Dr. Sussman suggested WBSR be used to treat patients with eating disorders, even though the label contraindication such use because of seizure risk.

135. GSK speakers Drs. Sarah Atkinson and Anita Clayton also recommended WBSR for weight loss in non-depressed patients, among other off-label uses. Dr. Jeffrey Green

presented WBSR as a treatment for cocaine and alcohol addictions and ADHD. In doing so, Dr. Green, also improperly minimized WBSR's FDA-required seizure risk. Dr. Croft recommended WBSR for the treatment of sexual dysfunction, for weight loss, ADD, chronic pain and children.

136. GSK representatives attended every PRIDE event and were well aware of the speakers' off-label claims. Leading speakers such as Drs. Pradko, Hudziak, Sussman, Clayton and Atkinson, Croft, and others spoke dozens of times a year and were highly sought after by GSK for such events. GSK used these speakers to promote off-label use of WBSR by frequently employing them as speakers, with full knowledge of the content of their presentations.

137. By at least October 2001, a GSK sales representative had notified senior GSK managers of the use of speaker programs to promote off-label uses, including to promote WBSR for children and ADHD and, in subsequent months, for weight loss. Exh. 22. The representative pointed out the evidence of the off-label speaker programs in his colleagues' call notes.

138. When this representative did not receive a response, he escalated his complaints to GSK's heads of human resources and compliance. In his complaint, the representative noted that he had "come forward with the truth, which could save the reputation of GSK, and millions of dollars in fines." Exh. 23. He later also wrote to GSK Chief Executives Robert Ingram and David Stout about his complaints. In early 2002, GSK initiated a compliance investigation that confirmed many of the representative's allegations, including the use of WBSR speaker programs to promote WBSR off-label and use of a spa program to entertain physicians.

139. The complaining sales representative was offered an unusually favorable severance package, including relocation payments and keeping the company car.

140. Although a manager admitted during GSK's internal investigation that he had been told by the sales representative that the speaker programs were off-label, and although another sales representative confirmed that the manager was aware of the off-label nature of the

programs, the manager received only a "verbal warning." Moreover, although the Chief Compliance Officer noted that off-label discussions by GSK speakers were "normal" (i.e. common) (Exh. 24), no action was taken to investigate further and the off-label promotion continued.

A. Sales Representatives Repeatedly Promoted Off-Label Uses of WBSR.

1. GSK Immersed Its Sales Force in Information on WBSR's Off-Label Uses.

141. GSK actively encouraged its sales force to promote WBSR for off-label uses. From the time of their introductory sales training and throughout their tenure with the company, sales representatives were bombarded with information about off-label uses of WBSR, including

Dr. Pradko's standard presentation at new representative sales training (every GSK sales representative who sold WBSR was also provided his or her own personal copy of Pradko's standard presentation, replete with off-label claims). Exh. 25.

142. Sales representatives were provided with multiple copies of the results of GSK-funded studies on weight loss in the non-depressed. For example, in June 2001, GSK distributed a memorandum to its WBSR sales force with new clinical data on the drug's impact on weight loss in non-depressed obese patients. GSK also distributed to its sales force the Gadde study and other studies of the use of WBSR in patients who did not have a diagnosis for depression.

143. GSK required the WBSR sales forces to take a home study course that included a review of studies on the off-label use of WBSR for weight loss. GSK required a mandatory written "knowledge certification" on the off-label weight loss data in non-depressed patients and other tests on off-label material about WBSR for ADHD.

144. Although representatives were "told" that they were not supposed to use this information affirmatively in promotion, they were required to "role-play" scenarios with their managers where they could use this off-label information. Moreover, their performance was

judged and their bonuses based on sales goals that reflected all sales, including off-label sales.

145. GSK sales representatives also proactively promoted the results of studies of non-depressed patients treated with WBSR for weight loss and sexual dysfunction despite the lack of any FDA-approval for these indications. Similarly, GSK directly promoted WBSR as an "add on" combination therapy to address SSRI-induced side effects, such as weight gain, sexual dysfunction, and so-called "poop out" or loss of energy. Thus, GSK's emphasis on various off-label uses translated into direct promotion to prescribing physicians by the company's sales representatives and was reflected year after year in the sales representatives' call notes. GSK took no action to correct the off-label marketing efforts documented in thousands of such call notes during the relevant time periods. The following are just a few of the many instances:

> "Killer detail today on SR. She wasn't seeming to know much about it but the line Happy Horny and Skinny was a good line for her today and we really got into the whole conversation" *2/1/01 Corvallis, OR*
>
> "…we talked about wsr in combo. with a ssri as well as using it in non depressed women for sexual dis" *2/16/01 Millstadt, IL*
>
> "Wants to golf; Reminder on Happy horny skinny pill;" *5/9/01 Bethel Park, PA*
>
> "Wellbutrin SR for the treatment of cocaine addiction." *8/9/01 Belle Mead, NJ*
>
> "Great conversation on WSR new wt loss study-augmenting for sex side affects-brought in rest of breakfast from NW health-loved it! Gave me more time to discuss the off label uses-ie Bipolar, ADD, Poop out." *8/20/01 Arlington Hghts., IL*
>
> "Nice follow up to last visit regarding use of WSR for anxiety, PTSD, ADD/ADHD, and social phobia." *9/26/01 Santa Fe, NM*
>
> "asked to prescribe in overweight pts also any pts with addictions need dopamine and wsr will give to them" *3/6/02 Trenton, NJ*
>
> "Quick positive points and talked about why I was there. Nondepressed women libido but he wouldn't bite." *3/11/02 Seattle, WA*
>
> "WBsr for your couch potatoes, happy, horny, skinny pill" *8/30/02 Folsom, CA*
>
> "Told him the "happy-horny-skinny" line which he loved. Makes it easier to